#### **RLL-193US**

#### **WE CLAIM:**

A compound having the structure of Formula I

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$$\underbrace{ \begin{array}{c} H & O \\ N-A-N \\ \end{array} }_{H} \underbrace{ \begin{array}{c} N-R \\ N-R \\ \end{array} }_{N-R}$$

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## FORMULA - I

its pharmaceutically acceptable salts, amides, enantiomers, diastereomers, N-oxides, prodrugs, metabolites or their polymorphs, wherein A is a straight or branched  $C_1$ - $C_4$  alkyl chain; R is cinnamyl, benzyl, substituted benzyl, phenyl, mono- or disubstituted phenyl group substituted with the substituents independently selected from the group consisting of halogen, hydroxy,  $C_1$ - $C_6$  alkoxy, trifluoromethyl, nitro, trifluoroalkoxy group, or (dihalodiphenyl) methyl,

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2. The compound according to claim 1 wherein halogen is selected from the group consisting of chloro, fluoro, iodo;  $C_1$ - $C_6$  alkyl is selected from the group consisting of methyl, ethyl, n-propyl, isopropyl, butyl, tert-butyl, and  $C_1$ - $C_6$  alkoxy is selected from the group consisting of methoxy, ethoxy, n-propoxy, isopropoxy, and hexyloxy.

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- 3. The compounds according to claim 1 selected from the group consisting of:
  - 2-[3-{4-(2-Methoxyphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 01).
  - 2-[3-{4-(3-Chlorophenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 02).
  - 2-[3-{4-(2-Methylphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 03).

- 2-[3-{4-(4-Fluorophenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 04).
- 2-[3-{4-(3-Trifluoromethylphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 05).
- 2-[3-{4-(2-Fluorophenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 06).
- 2-[3-{4-(3,4-Dimethylphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 07).
- 2-[3-{4-(2-Methoxy-5-fluorophenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 08).
- 2-[3-{4-(2-Ethylphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 09).
- 2-[3-{4-(2,4-Difluorophenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 10).
- 2-[3-{4-(2-Ethoxyphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 11).
- 2-[3-{4-(2-Methyl-5-chlorophenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 12).
- 2-[3-{4-(Phenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 13).
- 2-[3-{4-(Benzyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 14).
- 2-[3-{4-(Cinnamyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 15).
- 2-[3-{4-(4-Nitrophenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 16).
- 2-[3-{4-(3-Chloro-4-methylphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 17).
- 2-[3-{4-(4-Fluoro-2-methoxyphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 18).
- 2-[3-{4-(Bis-4-fluorophenyl)methylpiperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 19).
- 2-[3-{4-(2,4-Dichlorophenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 20).

- 2-[3-{4-(2,4-Dimethoxyphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 21).
- 2-[3-{4-(2,6-Dimethylphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 22).
- 2-[3-{4-(2-Isopropoxyphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 23).
- 2-[3-{4-(2-Propoxyphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 24).
- 2-[3-{4-(2-n-Hexyloxyphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 25).
- 2-[3-{4-(2,5-Dimethoxyphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 26).
- 2-[3-{4-(4-tert-Butylphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 27).
- 2-[3-{4-(2-Methoxy-6-hydroxyphenyl)piperazin-1-yl}propyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 28).
- 2-[3-{4-(2-Methoxyphenyl)piperazin-1-yl}-3-methylpropyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 29).
- 2-[3-{4-(2-Methoxyphenyl)piperazin-1-yl}-2-methylpropyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 30).
- 2-[3-{4-(2-Ethoxyphenyl)piperazin-1-yl}-3-methylpropyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (Compound 31).
- 4. A method of selectively antagonizing  $\alpha_1$ -adrenergic receptors in a mammal comprising administering to said mammal a compound having the structure of Formula I

N-A-N N-R

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its pharmaceutically acceptable salts, amides, enantiomers, diastereomers, Noxides, prodrugs, metabolites or their polymorphs, wherein A is a straight or branched  $C_1$ - $C_4$  alkyl chain; R is cinnamyl, benzyl, substituted benzyl, phenyl, mono- or disubstituted phenyl group substituted with the substituents independently selected from the group consisting of halogen, hydroxy,  $C_1$ - $C_6$  alkoxy, trifluoromethyl, nitro, trifluoroalkoxy group, or (dihalodiphenyl) methyl.

5. A method for treating benign prostatic hyperplasia in a mammal comprising administering to said mammal a compound having the structure of Formula I

$$\underbrace{ \left( \begin{array}{c} H & O \\ H & O \end{array} \right) }_{H} N-A-N \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R \end{array} \right) }_{N} N-R \underbrace{ \left( \begin{array}{c} N-R \\ N-R$$

# FORMULA - I

its pharmaceutically acceptable salts, amides, enantiomers, diastereomers, Noxides, prodrugs, metabolites or their polymorphs, wherein A is a straight or branched  $C_1$ - $C_4$  alkyl chain; R is cinnamyl, benzyl, substituted benzyl, phenyl, mono- or disubstituted with the substituents independently selected from the group consisting of halogen, hydroxy,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, trifluoromethyl, nitro, trifluoroalkoxy group, or (dihalodiphenyl) methyl.

6. A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutical acceptable carrier.

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A method of selectively antagonizing α<sub>1</sub>-adrenergic receptors in a
mammal comprising the step of administering to the said mammal the pharmaceutical composition according to claim 6.

- 8. A method for treating benign prostatic hyperplasia in a mammal comprising the step of administering to the said mammal the pharmaceutical composition according to claim 6.
- 9. A process for preparing a compound of Formula I

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$$\begin{array}{c|c} H & O \\ \hline & N-A-N \\ \hline & N-R \end{array}$$

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or its pharmaceutically acceptable salts, amides, enantiomers, diastereomers, N-oxides, prodrugs, metabolites or their polymorphs, wherein A is a straight or branched  $C_1$ - $C_4$  alkyl chain; R is cinnamyl, benzyl, substituted benzyl, phenyl, mono- or disubstituted phenyl group substituted with the substituents independently selected from the group consisting of halogen, hydroxy,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, trifluoromethyl, nitro, trifluoroalkoxy group, or (dihalodiphenyl) methyl, which comprises reacting a compound of Formula II, with piperazine derivatives of Formula III, as shown in Scheme I wherein A and R are the same as defined above.

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10. A process for preparing a compound of Formula I

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## FORMULA - I

or its pharmaceutically acceptable salts, amides, enantiomers, diastereomers, N-oxides, prodrugs, metabolites or their polymorphs, wherein A is a straight or

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branched  $C_1$ - $C_4$  alkyl chain; R is cinnamyl, benzyl, substituted benzyl, phenyl, mono- or disubstituted phenyl group substituted with the substituents independently selected from the group consisting of halogen, hydroxy,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, trifluoromethyl, nitro, trifluoroalkoxy group or (dihalodiphenyl) methyl, which comprises reacting 1-( $\omega$ -haloalkyl)cis-3a,4,7,7a-tetrahydrophthalimide of Formula IV, wherein A is the same as defined above, with a compound of Formula V, wherein R is the same as defined above, as shown in Scheme II.